

Modeling Diseases in NCI Thesaurus: Initial Model with Examples

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Goals

This model of neoplasms and related diseases addresses two basic needs:

1. To define, code, and retrieve neoplasms according to their essential aspects and criteria; and
2. To represent known but weaker associations – such as normal, indicative, and experimentally associated findings – important for both clinical and research purposes.

Definitional aspects are most important, both to our understanding of cancer and to ensure the logical integrity of disease concepts. How much non-definitional data can and should go in the terminology remains an open question.

Relating Disease Concepts to Defining and Associated Features

Defining roles for neoplasms are criteria used to make the diagnosis. Such assertions should hold true for all subtypes, so inherited values remain valid; values will often be more narrowly restricted for particular subtypes. Initial defining roles:

All*	Disease_Has_Associated_Anatomic_Site	<Anatomy>
All	Disease_Has_Primary_Anatomic_Site	<Anatomy>
All	Disease_Has_Metastatic_Anatomic_Site	<Anatomy>
All	Disease_Has_Normal_Tissue_Origin	<Anatomy: Tissue>
All*	Disease_Has_Normal_Cell_Origin	<Anatomy: Normal Cell>
All	Disease_Has_Abnormal_Cell	<Abnormal Cell>
All	Disease_Has_Molecular_Abnormality	<Molecular Abnormality>
All	Disease_Has_Cytogenetic_Abnormality	<Molecular Abnormality: Cytogenetic Abnormality>
All	Disease_Has_Finding	<Findings and Disorders: Finding>
All	Disease_Is_Stage	<Property/Attribute: Disease Stage Modifier>
All	Disease_Is_Grade	<Property/Attribute: Disease Grade Modifier>

* “Some” may be needed in Apelon software for mixed values (e.g. associated sites for metastases, normal tissue/cell of mixed tumors).

Non-defining roles for neoplasms reflect significant associations which are not true for all instances. This is indicated in the logic by the “Some” qualifier, and to users by the “May_Have” role names. Inherited values should still remain broadly true; if *some* becomes *none* for some subtypes, it is preferable to assert only at subtype level (availability of negation could change this).

Some	Disease_May_Have_Normal_Tissue_Origin	<Anatomy: Tissue>
Some	Disease_May_Have_Normal_Cell_Origin	<Anatomy: Normal Cell>
Some	Disease_May_Have_Abnormal_Cell	<Abnormal Cell>
Some	Disease_May_Have_Molecular_Abnormality	<Molecular Abnormality>
Some	Disease_May_Have_Cytogenetic_Abnormality	<Molecular Abnormality: Cytogenetic Abnormality>
Some	Disease_May_Have_Finding	<Findings and Disorders: Finding>
Some	Disease_May_Have_Associated_Disease	<Findings and Disorders: Diseases and Disorders>

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Lymphoma Examples Applying the Model

Note: Only select concepts and roles/values are shown, to illustrate various aspects.
Roles/values are shown only where introduced, and inherit down.

- 1 Lymphoma
 - 1.1 Hodgkin's Lymphoma
 - 1.1.1 Nodular Lymphocyte Predominant Hodgkin's Lymphoma
 - 1.2 Mature B-Cell Non-Hodgkin's Lymphoma
 - 1.2.1 Mantle Cell Lymphoma
 - 1.2.2 Diffuse Large B-Cell Lymphoma (DLBCL)
 - 1.2.2.1 Diffuse Large B-Cell Lymphoma with a Germinal Center B-Cell Expression Profile (GCB-DLBCL)
 - 1.2.2.2 Diffuse Large B-Cell Lymphoma with an Activated B-Cell Expression Profile (ABC-DLBCL)
 - 1.2.2.3 Centroblastic Lymphoma
 - 1.2.2.4 Immunoblastic Lymphoma

1 Lymphoma

All	Disease_Has_Primary_Anatomic_Site	Organ System
All	Disease_Has_Normal_Cell_Origin	Lymphocyte
All	Disease_Has_Abnormal_Cell	Neoplastic Lymphocyte

1.1 Hodgkin's Lymphoma

[one or other value]

Some	Disease_Has_Normal_Cell_Origin	B-Cell [omit or children only]
Some	Disease_Has_Normal_Cell_Origin	T-Cell [omit or children only]

1.1.1 Nodular Lymphocyte Predominant Hodgkin's Lymphoma

[inherits from Hodgkin's Lymphoma above, but 100% B-Cell]

All	Disease_Has_Normal_Cell_Origin	B-Cell
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1.2 Mature B-Cell Non-Hodgkin's Lymphoma

All	Disease_Has_Normal_Cell_Origin	Mature B-Cell
All	Disease_Has_Molecular_Abnormality	Clonal Immunoglobulin Heavy Chain Gene Rearrangement
All	Disease_Has_Molecular_Abnormality	Clonal Immunoglobulin Light Chain Gene Rearrangement

1.2.1 Mantle Cell Lymphoma

All	Disease_Has_Primary_Anatomic_Site	Lymphatic System
All	Disease_Has_Normal_Tissue_Origin	Mantle Zone
All	Disease_Has_Normal_Cell_Origin	Mature B-Lymphocyte
All	Disease_Has_Abnormal_Cell	Centrocyte
All	Disease_Has_Cytogenetic_Abnormality	t(11;14)(q13;q32) Chromosomal Translocation
All	Disease_Has_Molecular_Abnormality	Monoclonal BCL-1 Gene Rearrangement
All	Disease_Has_Molecular_Abnormality	Cyclin D1 mRNA Overexpression

[most patients:]

Some	Disease_May_Have_Finding	Lymphadenopathy
Some	Disease_May_Have_Finding	Hepatomegaly
Some	Disease_May_Have_Finding	Splenomegaly

[none or one of:]

Some	Disease_May_Have_Cytogenetic_Abnormality	Trisomy 12
Some	Disease_May_Have_Cytogenetic_Abnormality	del(13q14)
Some	Disease_May_Have_Cytogenetic_Abnormality	del(17p)

1.2.2 Diffuse Large B-Cell Lymphoma (DLBCL)

All	Disease_Has_Finding	Rapidly Enlarging Mass
All	Disease_Has_Morphologic_Finding	Diffuse Pattern

1.2.2.1 Diffuse Large B-Cell Lymphoma with a Germinal Center B-Cell Expression Profile (GCB-DLBCL)

All	Disease_Has_Finding	Favorable Clinical Outcome
All	Disease_Has_Cytogenetic_Abnormality	t(14;18)(q32;q21)
All	Disease_Has_Molecular_Abnormality	BCL-6 Gene Expression
All	Disease_Has_Molecular_Abnormality	LMO2 Gene Expression
All	Disease_Has_Molecular_Abnormality	A-myb Gene Expression
Some	Disease_May_Have_Normal_Cell_Origin	Large Non-Cleaved Cell (Centroblast)
Some	Disease_May_Have_Normal_Cell_Origin	B-Immunoblast
Some	Disease_May_Have_Abnormal_Cell	Neoplastic Large Non-Cleaved Cell (Neoplastic Centroblast)
Some	Disease_May_Have_Abnormal_Cell	Neoplastic B-Immunoblast
Some	Disease_May_Have_Abnormal_Cell	Multilobated Neoplastic B Lymphocyte

1.2.2.2 Diffuse Large B-Cell Lymphoma with an Activated B-Cell Expression Profile (ABC-DLBCL)

All	Disease_Has_Normal_Cell_Origin	Memory B-Lymphocyte
All	Disease_Has_Finding	Aggressive Clinical Course
All	Disease_Has_Molecular_Abnormality	Increased NFkappa Pathway Activation
All	Disease_Has_Molecular_Abnormality	BCL-2 Gene Expression
All	Disease_Has_Molecular_Abnormality	CD44 Gene Expression
Some	Disease_May_Have_Normal_Cell_Origin	Large Non-Cleaved Cell (Centroblast)
Some	Disease_May_Have_Normal_Cell_Origin	B-Immunoblast
Some	Disease_May_Have_Abnormal_Cell	Neoplastic Large Non-Cleaved Cell (Neoplastic Centroblast)
Some	Disease_May_Have_Abnormal_Cell	Neoplastic B-Immunoblast

1.2.2.3 Centroblastic Lymphoma

All	Disease_Has_Abnormal_Cell	Neoplastic Large Non-Cleaved Cell (Neoplastic Centroblast)
All	Disease_Has_Finding	Aggressive Clinical Course

1.2.2.4 Immunoblastic Lymphoma

All	Disease_Has_Abnormal_Cell	Neoplastic B-Immunoblast ($\geq 90\%$)
All	Disease_Has_Finding	Aggressive Clinical Course

Myelodysplastic Syndrome Examples

Myelodysplastic Syndrome

All Disease_Has_Associated_Anatomic_Site Bone Marrow
All Disease_Has_Associated_Anatomic_Site Blood
All Disease_Has_Primary_Anatomic_Site Bone Marrow
All Disease_Has_Normal_Cell_Origin Bone Marrow Stem Cell
All Disease_Has_Abnormal_Cell Clonal Hematopoietic Stem Cell
All Disease_Has_Finding Ineffective Hematopoiesis Present
All Disease_Has_Finding Bone Marrow Dysplasia Present
All Disease_Has_Finding Myeloblasts Under 20 Percent of Bone Marrow Nucleated Cells
All Disease_Has_Finding Myeloblasts Under 20 Percent of Peripheral Blood White Cells

Refractory Anemia

All Disease_Has_Abnormal_Cell Dysplastic Erythroblast
Some Disease_May_Have_Abnormal_Cell Megaloblast
Some Disease_May_Have_Abnormal_Cell Ringed Sideroblast
All Disease_Has_Finding Myeloblasts Under 1 Percent of Peripheral Blood White Cells
All Disease_Has_Finding Myeloblasts Under 5 Percent of Bone Marrow Nucleated Cells
All Disease_Has_Finding Ringed Sideroblasts Under 15 Percent of Erythroid Precursors
Some Disease_May_Have_Finding Hypercellular Bone Marrow
Some Disease_May_Have_Finding Anisocytosis
Some Disease_May_Have_Finding Poikilocytosis
Some Disease_May_Have_Cytogenetic_Abnormality del(20q)
Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 8
All Disease_Is Low Risk

Refractory Anemia with Ringed Sideroblasts

All Disease_Has_Abnormal_Cell Dysplastic Erythroblast
All Disease_Has_Abnormal_Cell Ringed Sideroblast
Some Disease_May_Have_Abnormal_Cell Megaloblast
All Disease_Has_Finding Ringed Sideroblasts 15 Percent or More of Erythroid Precursors
All Disease_Has_Finding Myeloblasts Under 5 Percent of Bone Marrow Nucleated Cells
Some Disease_May_Have_Finding Anisochromasia
Some Disease_May_Have_Finding Hypercellular Bone Marrow
Some Disease_May_Have_Finding Hemosiderin-Laden Macrophage
All Disease_Is Low Risk

Refractory Cytopenia with Multilineage Dysplasia

Some Disease_May_Have_Abnormal_Cell Dysplastic Erythroblast
Some Disease_May_Have_Abnormal_Cell Large Multinucleated Erythroid Cell
Some Disease_May_Have_Abnormal_Cell Megaloblast
Some Disease_May_Have_Abnormal_Cell Dysplastic Granulocyte
Some Disease_May_Have_Abnormal_Cell Dysplastic Neutrophil
Some Disease_May_Have_Abnormal_Cell Neutrophil with Pseudo Pelger-Huet Nucleus
Some Disease_May_Have_Abnormal_Cell Hypolobated Megakaryocyte
Some Disease_May_Have_Abnormal_Cell Micromegakaryocyte
All Disease_Has_Finding Bone Marrow Dysplasia Present in 10 Percent or More of the Cells of Two Cell Lines
All Disease_Has_Finding Myeloblasts Under 5 Percent of Bone Marrow Nucleated Cells
All Disease_Has_Finding Myeloblasts Under 1 Percent of Peripheral Blood White Cells
Some Disease_May_Have_Finding Neutropenia
Some Disease_May_Have_Finding Thrombocytopenia
Some Disease_May_Have_Finding Trisomy 8
Some Disease_May_Have_Finding Monosomy 7
Some Disease_May_Have_Finding del(7q)
Some Disease_May_Have_Finding Monosomy 5
Some Disease_May_Have_Finding del(20q)
All Disease_Is High Risk

Refractory Cytopenia with Multilineage Dysplasia and Ringed Sideroblasts

All Disease_Has_Finding Ringed Sideroblasts 15 Percent or More of Erythroid Precursors

Refractory Anemia with Excess Blasts

Some Disease_May_Have_Abnormal_Cell Dysplastic Erythroblast
Some Disease_May_Have_Abnormal_Cell Large Multinucleated Erythroid Cell
Some Disease_May_Have_Abnormal_Cell Megaloblast
Some Disease_May_Have_Abnormal_Cell Dysplastic Granulocyte
Some Disease_May_Have_Abnormal_Cell Dysplastic Neutrophil
Some Disease_May_Have_Abnormal_Cell Neutrophil with Pseudo Pelger-Huet Nucleus
Some Disease_May_Have_Abnormal_Cell Neutrophil with Pseudo Chediak-Higashi Granules
Some Disease_May_Have_Abnormal_Cell Hypolobated Megakaryocyte

Some Disease_May_Have_Abnormal_Cell Micromegakaryocyte
 Some Disease_May_Have_Finding Myeloblasts 5-19 Percent of Bone Marrow Nucleated Cells [Note RAEB-2 exceptional cases]
 Some Disease_May_Have_Finding Neutropenia
 Some Disease_May_Have_Finding Thrombocytopenia
 Some Disease_May_Have_Finding Anisopoikilocytosis
 Some Disease_May_Have_Finding Abnormal Platelet
 Some Disease_May_Have_Finding Hypercellular Bone Marrow
 Some Disease_May_Have_Finding Hypocellular Bone Marrow
 Some Disease_May_Have_Finding del(20q)
 Some Disease_May_Have_Finding del(7q)
 Some Disease_May_Have_Finding Gain of Chromosome 8
 Some Disease_May_Have_Finding Monosomy 5
 All Disease_Is High Risk

RAEB-1

All Disease_Has_Finding Myeloblasts 5-9 Percent of Bone Marrow Nucleated Cells
 All Disease_Has_Finding Myeloblasts Under 5 Percent of Peripheral Blood White Cells

RAEB-2 [Note: Either the 1st is true, or in rare cases conditions 2 and 3 are true:]

Some Disease_May_Have_Finding Myeloblasts 10-19 Percent of Bone Marrow Nucleated Cells
 Some Disease_May_Have_Finding Myeloblasts Under 10 Percent of Bone Marrow Nucleated Cells
 Some Disease_May_Have_Finding Myeloblasts 5-19 Percent of Peripheral Blood White Cells
 Some Disease_May_Have_Finding Auer Rods Present

Myelodysplastic Syndrome Associated with Isolated del(5q) Chromosome Abnormality

All Disease_Has_Abnormal_Cell Dysplastic Erythroblast
 Some Disease_May_Have_Abnormal_Cell Hypolobated Megakaryocyte
 All Disease_Has_Finding Myeloblasts Under 5 Percent of Bone Marrow Nucleated Cells
 All Disease_Has_Finding Myeloblasts Under 5 Percent of Peripheral Blood White Cells
 Some Disease_May_Have_Finding Leukopenia
 Some Disease_May_Have_Finding Thrombocytosis
 Some Disease_May_Have_Finding Hypercellular Bone Marrow
 Some Disease_May_Have_Finding Megakaryocytes Increased
 All Disease_Has_Finding del(5q)
 All Disease_Is Low Risk

Myelodysplastic Syndrome, Unclassifiable

Some Disease_May_Have_Abnormal_Cell Dysplastic Granulocyte
 Some Disease_May_Have_Abnormal_Cell Dysplastic Neutrophil
 Some Disease_May_Have_Abnormal_Cell Dysplastic Megakaryocyte
 All Disease_Has_Finding Myeloblasts Under 5 Percent of Bone Marrow Nucleated Cells
 All Disease_Has_Finding Myeloblasts Under 1 Percent of Peripheral Blood White Cells
 Some Disease_May_Have_Finding Neutropenia
 Some Disease_May_Have_Finding Thrombocytopenia
 Some Disease_May_Have_Finding Hypercellular Bone Marrow
 Some Disease_May_Have_Finding Hypocellular Bone Marrow

de novo Myelodysplastic Syndrome

Some Disease_May_Have_Finding Benzene Exposure

Secondary Myelodysplastic Syndrome

Therapy-Related Myelodysplastic Syndrome

Epipodophyllotoxin-Related Myelodysplastic Syndrome

Alkylating Agent-Related Myelodysplastic Syndrome

Some Disease_May_Have_Abnormal_Cell Dysplastic Erythroblast
 Some Disease_May_Have_Abnormal_Cell Dysplastic Granulocyte
 Some Disease_May_Have_Abnormal_Cell Dysplastic Neutrophil
 Some Disease_May_Have_Abnormal_Cell Dysplastic Megakaryocyte
 Some Disease_May_Have_Finding Ringed Sideroblasts 15 Percent or More of Erythroid Precursors
 Some Disease_May_Have_Finding Auer Rods Present
 Some Disease_May_Have_Finding Pancytopenia
 Some Disease_May_Have_Finding Neutropenia
 Some Disease_May_Have_Finding Thrombocytopenia
 Some Disease_May_Have_Finding Hypercellular Bone Marrow
 Some Disease_May_Have_Finding Hypocellular Bone Marrow
 Some Disease_May_Have_Finding Bone Marrow Basophilia
 Some Disease_May_Have_Finding Bone Marrow Fibrosis
 All Disease_Is High Risk

Previously Treated Myelodysplastic Syndrome

Epithelial Hepatic and Intrahepatic Bile Duct Examples

Epithelial Hepatic and Intrahepatic Bile Duct Neoplasm

All Disease_Has_Associated_Anatomic_Site Gastrointestinal System

All Disease_Has_Primary_Anatomic_Site Gastrointestinal System

All Disease_Has_Normal_Cell_Origin Epithelial Cell

All Disease_Has_Abnormal_Cell Neoplastic Epithelial Cell

Liver and Intrahepatic Biliary Tract Carcinoma

All Disease_Has_Abnormal_Cell Malignant Epithelial Cell

Hepatocellular Carcinoma

All Disease_Has_Associated_Anatomic_Site Liver

All Disease_Has_Primary_Anatomic_Site Liver

All Disease_Has_Normal_Tissue_Origin Hepatic Tissue

All Disease_Has_Normal_Cell_Origin Hepatocyte

All Disease_Has_Abnormal_Cell Adenocarcinoma Cell

Some Disease_May_Have_Abnormal_Cell Pleomorphic Adenocarcinoma Cell

Some Disease_May_Have_Abnormal_Cell Adenocarcinoma Spindle Cell

Some Disease_May_Have_Abnormal_Cell Giant Adenocarcinoma Cell

Some Disease_May_Have_Abnormal_Cell Adenocarcinoma Clear Cell

Some Disease_May_Have_Abnormal_Cell Poorly Differentiated Adenocarcinoma Cell

Some Disease_May_Have_Abnormal_Cell Polygonal Adenocarcinoma Cell with Eosinophilic Cytoplasm

Some Disease_May_Have_Abnormal_Cell Adenocarcinoma Cell with Eosinophilic Granular Cytoplasm

Some Disease_May_Have_Finding Abdominal Pain

Some Disease_May_Have_Finding Malaise

Some Disease_May_Have_Finding Weight Loss

Some Disease_May_Have_Finding Hepatomegaly

Some Disease_May_Have_Finding Ascites

Some Disease_May_Have_Finding Splenomegaly

Some Disease_May_Have_Finding Fever

Some Disease_May_Have_Finding Jaundice

Some Disease_May_Have_Finding Aspartate Aminotransferase Increased

Some Disease_May_Have_Finding Alanine Aminotransferase Increased

Some Disease_May_Have_Finding Gamma Glutamyltransferase Increased

Some Disease_May_Have_Finding Alpha Fetoprotein Increased

Some Disease_May_Have_Finding Trabecular Pattern

Some Disease_May_Have_Finding Pseudoglandular Pattern

Some Disease_May_Have_Finding Acinar Pattern

Some Disease_May_Have_Finding Compact Pattern

Some Disease_May_Have_Finding Schirrous Pattern

Some Disease_May_Have_Finding Fatty Change

Some Disease_May_Have_Finding Mallory Body

Some Disease_May_Have_Finding Ground Glass Nuclear Inclusion

Some Disease_May_Have_Finding Globular Hyaline Body

All Disease_Has_Molecular_Abnormality Monoclonal Hepatocyte Population

Some Disease_May_Have_Molecular_Abnormality P53 Tumor-Suppressor Gene Inactivation

Some Disease_May_Have_Molecular_Abnormality CCND1 Gene Amplification

Some Disease_May_Have_Molecular_Abnormality Cyclin D1 Protein Overexpression

Some Disease_May_Have_Molecular_Abnormality Cyclin D1 Messenger RNA Overexpression

Some Disease_May_Have_Molecular_Abnormality Cyclin E Protein Overexpression

Some Disease_May_Have_Molecular_Abnormality Beta Catenin Gene Mutation

Some Disease_May_Have_Molecular_Abnormality Transforming Growth Factor-Beta Overexpression

Some Disease_May_Have_Molecular_Abnormality Basic Fibroblast Growth Factor Overexpression

Some Disease_May_Have_Molecular_Abnormality Acidic Fibroblast Growth Factor Overexpression

Some Disease_May_Have_Molecular_Abnormality Aberrant DNA Methylation

Some Disease_May_Have_Cytogenetic_Abnormality del(1p)

Some Disease_May_Have_Cytogenetic_Abnormality del(4q)

Some Disease_May_Have_Cytogenetic_Abnormality del(5q)

Some Disease_May_Have_Cytogenetic_Abnormality del(8p)

Some Disease_May_Have_Cytogenetic_Abnormality del(13q)

Some Disease_May_Have_Cytogenetic_Abnormality del(16q)
 Some Disease_May_Have_Cytogenetic_Abnormality del(17p)
 Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 8
 Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 20
 Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome X
 Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 6
 Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 18
 Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 3
 Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 16
 Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 10
 Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 17

Fibrolamellar Hepatocellular Carcinoma

All Disease_Has_Abnormal_Cell Adenocarcinoma Cell with Eosinophilic Granular Cytoplasm
 All Disease_Has_Abnormal_Cell Polygonal Adenocarcinoma Cell with Eosinophilic Cytoplasm
 All Disease_Has_Finding Trabecular Pattern

Intrahepatic Cholangiocarcinoma

All Disease_Has_Associated_Anatomic_Site Intrahepatic Bile Duct
 All Disease_Has_Primary_Anatomic_Site Intrahepatic Bile Duct
 All Disease_Has_Normal_Tissue_Origin Columnar Epithelium
 All Disease_Has_Normal_Cell_Origin Columnar Cell
 All Disease_Has_Abnormal_Cell Adenocarcinoma Cell
 Some Disease_May_Have_Abnormal_Cell Pleomorphic Adenocarcinoma Cell
 Some Disease_May_Have_Abnormal_Cell Adenocarcinoma Clear Cell
 Some Disease_May_Have_Finding Thorotrast Exposure
 Some Disease_May_Have_Finding Abdominal Pain
 Some Disease_May_Have_Finding Malaise
 Some Disease_May_Have_Finding Weight Loss
 Some Disease_May_Have_Finding Multinodular Mass
 Some Disease_May_Have_Molecular_Abnormality P53 Tumor-Suppressor Gene Inactivation
 Some Disease_May_Have_Molecular_Abnormality KRAS Gene Amplification

Hepatocellular Adenoma

All Disease_Has_Associated_Anatomic_Site Liver
 All Disease_Has_Normal_Tissue_Origin Hepatic Tissue
 All Disease_Has_Normal_Cell_Origin Hepatocyte
 All Disease_Has_Abnormal_Cell Neoplastic Glandular Cell
 Some Disease_May_Have_Finding Necrotic Change
 Some Disease_May_Have_Finding Fibrosis
 Some Disease_May_Have_Finding Hemorrhagic Change

Hepatic Carcinoid Tumor

All Disease_Has_Associated_Anatomic_Site Liver
 All Disease_Has_Primary_Anatomic_Site Liver
 All Disease_Has_Normal_Tissue_Origin Hepatic Tissue
 All Disease_Has_Normal_Cell_Origin Argentaffin Cell
 All Disease_Has_Abnormal_Cell Malignant Neuroendocrine Cell
 All Disease_Has_Finding Neurosecretory Granule
 Some Disease_May_Have_Finding Insular Pattern
 Some Disease_May_Have_Finding Trabecular Pattern
 Some Disease_May_Have_Finding Glandular Pattern

Childhood Liver Cancer

All Disease_Has_Associated_Anatomic_Site Liver
 All Disease_Has_Primary_Anatomic_Site Liver
 All Disease_Has_Normal_Tissue_Origin Hepatic Tissue
 All Disease_Has_Normal_Cell_Origin Hepatocyte
 All Disease_Has_Abnormal_Cell Malignant Epithelial Cell

Hepatoblastoma

Some Disease_May_Have_Abnormal_Cell Neoplastic Small Round Cell
 Some Disease_May_Have_Abnormal_Cell Malignant Epithelial Large Cell
 Some Disease_May_Have_Abnormal_Cell Neoplastic Spindle Cell
 Some Disease_May_Have_Finding Thrombocytosis
 Some Disease_May_Have_Finding Enlarging Abdomen

Some Disease_May_Have_Finding Alpha Fetoprotein Increased
 Some Disease_May_Have_Finding Blood Alkaline Phosphatase Increased
 Some Disease_May_Have_Finding Fetal-Epithelial Differentiation
 Some Disease_May_Have_Finding Mesenchymal Differentiation
 Some Disease_May_Have_Finding Macrotrabecular Pattern
 Some Disease_May_Have_Cytogenetic_Abnormality Trisomy 2
 Some Disease_May_Have_Cytogenetic_Abnormality Trisomy 20
 All_Disease_Is_Stage Hepatoblastoma Stage

Bile Duct Adenocarcinoma

All Disease_Has_Associated_Anatomic_Site Bile Duct
 All Disease_Has_Associated_Anatomic_Site Bile Duct
 All Disease_Has_Normal_Tissue_Origin Columnar Epithelium
 All Disease_Has_Normal_Cell_Origin Columnar Cell
 All Disease_Has_Abnormal_Cell Adenocarcinoma Cell

Cholangiocarcinoma

Some Disease_May_Have_Abnormal_Cell Pleomorphic Adenocarcinoma Cell
 Some Disease_May_Have_Abnormal_Cell Adenocarcinoma Clear Cell
 Some Disease_May_Have_Finding Thorotrast Exposure
 Some Disease_May_Have_Finding Abdominal Pain
 Some Disease_May_Have_Finding Malaise
 Some Disease_May_Have_Finding Weight Loss
 Some Disease_May_Have_Finding Multinodular Mass
 Some Disease_May_Have_Molecular_Abnormality P53 Tumor-Suppressor Gene Inactivation
 Some Disease_May_Have_Molecular_Abnormality KRAS Gene Amplification

Intrahepatic Cholangiocarcinoma

All Disease_Has_Associated_Anatomic_Site Intrahepatic Bile Duct
 All Disease_Has_Primary_Anatomic_Site Intrahepatic Bile Duct
 All Disease_Has_Normal_Tissue_Origin Columnar Epithelium
 All Disease_Has_Normal_Cell_Origin Columnar Cell
 All Disease_Has_Abnormal_Cell Adenocarcinoma Cell
 Some Disease_May_Have_Abnormal_Cell Pleomorphic Adenocarcinoma Cell
 Some Disease_May_Have_Abnormal_Cell Adenocarcinoma Clear Cell
 Some Disease_May_Have_Finding Thorotrast Exposure
 Some Disease_May_Have_Finding Abdominal Pain
 Some Disease_May_Have_Finding Malaise
 Some Disease_May_Have_Finding Weight Loss
 Some Disease_May_Have_Finding Multinodular Mass
 Some Disease_May_Have_Molecular_Abnormality P53 Tumor-Suppressor Gene Inactivation
 Some Disease_May_Have_Molecular_Abnormality KRAS Gene Amplification

Hilar Cholangiocarcinoma

All Disease_Has_Associated_Anatomic_Site Hepatic Duct
 All Disease_Has_Primary_Anatomic_Site Hepatic Duct

Extrahepatic Bile Duct Adenocarcinoma

All Disease_Has_Associated_Anatomic_Site Extrahepatic Bile Duct
 All Disease_Has_Primary_Anatomic_Site Extrahepatic Bile Duct

Breast Carcinoma Examples

Breast Carcinoma

All Disease_Has_Associated_Anatomic_Site Breast
All Disease_Has_Primary_Anatomic_Site Breast
All Disease_Has_Normal_Tissue_Origin Breast Tissue
All Disease_Has_Normal_Cell_Origin Epithelial Cell
All Disease_Has_Abnormal_Cell Malignant Epithelial Cell
Some Disease_May_Have_Finding Breast Lump
Some Disease_May_Have_Finding Calcification
Some Disease_May_Have_Finding Microcalcification
Some Disease_May_Have_Molecular_Abnormality EGFR Gene Amplification
Some Disease_May_Have_Molecular_Abnormality FGFR1 Gene Amplification
Some Disease_May_Have_Molecular_Abnormality c-myc Gene Amplification
Some Disease_May_Have_Molecular_Abnormality FGFR2 Gene Amplification
Some Disease_May_Have_Molecular_Abnormality CCND1 Gene Amplification
Some Disease_May_Have_Molecular_Abnormality Cyclin D1 Protein Overexpression
Some Disease_May_Have_Molecular_Abnormality Cyclin D1 Messenger RNA Overexpression
Some Disease_May_Have_Molecular_Abnormality RB1 Tumor Suppressor Gene Inactivation
Some Disease_May_Have_Molecular_Abnormality c-erbB2 Gene Amplification
Some Disease_May_Have_Molecular_Abnormality c-erbB2 Protein Overexpression
Some Disease_May_Have_Molecular_Abnormality c-erbB2 messenger RNA Overexpression
Some Disease_May_Have_Molecular_Abnormality IGF2R Tumor Suppressor Gene Inactivation
Some Disease_May_Have_Molecular_Abnormality TP53 Tumor Suppressor Gene Inactivation

Breast Adenocarcinoma

All Disease_Has_Normal_Tissue_Origin Terminal Ductal Lobular Unit
All Disease_Has_Normal_Cell_Origin Terminal Ductal Lobular Unit Cell
All Disease_Has_Abnormal_Cell Adenocarcinoma Cell
Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 1q
Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 6q
Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 8q
Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 17q
Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 19q
Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 20q
Some Disease_May_Have_Cytogenetic_Abnormality Gain of ChromosomeXq,
Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 8p
Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 13q
Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 16q
Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 17p
Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 22q

Tubular Breast Carcinoma

All Disease_Has_Finding Tubular Pattern
Some Disease_May_Have_Finding Desmoplastic Stroma Formation
Some Disease_May_Have_Finding Stellate Configuration
Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 11q ATM Gene Locus
Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 3p FHIT Gene Locus

Ductal Breast Carcinoma

All Disease_Has_Abnormal_Cell Ductal Carcinoma Cell

Ductal Carcinoma In Situ of the Breast

Some Disease_May_Have_Abnormal_Cell Adenocarcinoma Spindle Cell
Some Disease_May_Have_Abnormal_Cell Adenocarcinoma Clear Cell
Some Disease_May_Have_Abnormal_Cell Signet Ring Adenocarcinoma Cell
Some Disease_May_Have_Finding Nipple Discharge
Some Disease_May_Have_Finding Multifocal Lesion
Some Disease_May_Have_Finding Psammoma Body Formation
Some Disease_May_Have_Finding Paget Involvement
Some Disease_May_Have_Finding Cribriform Pattern
Some Disease_May_Have_Finding Micropapillary Pattern
Some Disease_May_Have_Finding Solid Pattern
Some Disease_May_Have_Cytogenetic_Abnormality Polysomy 3

Some Disease_May_Have_Cytogenetic_Abnormality Polysomy 10
 Some Disease_May_Have_Cytogenetic_Abnormality Polysomy 17
 Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 1
 Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 18
Invasive Ductal Carcinoma, not Otherwise Specified
 Some Disease_May_Have_Abnormal_Cell Pleomorphic Epithelial Cell
 Some Disease_May_Have_Finding Firm Mass
 Some Disease_May_Have_Finding Trabecular Pattern
 Some Disease_May_Have_Finding Solid Pattern
 Some Disease_May_Have_Finding Syncytial Pattern
 Some Disease_May_Have_Finding Necrotic Change
Lobular Breast Carcinoma
 All Disease_Has_Abnormal_Cell Lobular Carcinoma Cell
 Some Disease_May_Have_Abnormal_Cell Pleomorphic Epithelial Cell
 Some Disease_May_Have_Finding Bilateral Mass
 Some Disease_May_Have_Finding Apocrine Metaplasia
 Some Disease_May_Have_Molecular_Abnormality Loss of E-cadherin Expression
 Some Disease_May_Have_Molecular_Abnormality CDH1 Tumor Suppressor Gene Inactivation
Lobular Carcinoma In Situ of the Breast
 Some Disease_May_Have_Finding Multifocal Lesion
 Some Disease_May_Have_Finding Paget Involvement
 Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 16p
Invasive Lobular Breast Carcinoma
 All Disease_Has_Finding Single File Linear Pattern
 All Disease_Has_Finding Fibrotic Stroma Formation
Mixed Lobular and Ductal Breast Carcinoma
 Some Disease_May_Have_Molecular_Abnormality Loss of E-cadherin Expression
Invasive Breast Carcinoma
 Some Disease_May_Have_Cytogenetic_Abnormality i(1)(q10),
 Some Disease_May_Have_Cytogenetic_Abnormality i(8)(q10)
 Some Disease_May_Have_Cytogenetic_Abnormality der(1;16)(q10;p10)
Tubular Breast Carcinoma
 All Disease_Has_Finding Tubular Pattern
 Some Disease_May_Have_Finding Desmoplastic Stroma Formation
 Some Disease_May_Have_Finding Stellate Configuration
 Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 11q ATM Gene Locus
 Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome 3p FHIT Gene Locus
Invasive Ductal Carcinoma, not Otherwise Specified
 Some Disease_May_Have_Abnormal_Cell Pleomorphic Epithelial Cell
 Some Disease_May_Have_Finding Firm Mass
 Some Disease_May_Have_Finding Trabecular Pattern
 Some Disease_May_Have_Finding Solid Pattern
 Some Disease_May_Have_Finding Syncytial Pattern
 Some Disease_May_Have_Finding Necrotic Change
Invasive Lobular Breast Carcinoma
 All Disease_Has_Finding Single File Linear Pattern
 All Disease_Has_Finding Fibrotic Stroma Formation
Female Breast Carcinoma
Hereditary Female Breast Carcinoma
 Some Disease_May_Have_Molecular_Abnormality BRCA 1 Mutation
Male Breast Carcinoma
 Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome X
 Some Disease_May_Have_Cytogenetic_Abnormality Loss of Chromosome Y
 Some Disease_May_Have_Cytogenetic_Abnormality Gain of Chromosome 5
Hereditary Male Breast Carcinoma
Hereditary Breast Carcinoma
 Some Disease_May_Have_Molecular_Abnormality BRCA 2 Mutation
Hereditary Female Breast Carcinoma
 Some Disease_May_Have_Molecular_Abnormality BRCA 1 Mutation
Hereditary Male Breast Carcinoma

Sporadic Breast Carcinoma

Some Disease_May_Have_Cytogenetic_Abnormality	Trisomy 7
Some Disease_May_Have_Cytogenetic_Abnormality	Trisomy 18
Some Disease_May_Have_Cytogenetic_Abnormality	Monosomy 6
Some Disease_May_Have_Cytogenetic_Abnormality	Monosomy 8
Some Disease_May_Have_Cytogenetic_Abnormality	Monosomy 11
Some Disease_May_Have_Cytogenetic_Abnormality	Monosomy 13
Some Disease_May_Have_Cytogenetic_Abnormality	Monosomy 16
Some Disease_May_Have_Cytogenetic_Abnormality	Monosomy 17
Some Disease_May_Have_Cytogenetic_Abnormality	Monosomy 22
Some Disease_May_Have_Cytogenetic_Abnormality	Monosomy X
Some Disease_May_Have_Cytogenetic_Abnormality	Loss of Chromosome 17
Some Disease_May_Have_Cytogenetic_Abnormality	Loss of Chromosome 6q
Some Disease_May_Have_Cytogenetic_Abnormality	Loss of Chromosome 19
Some Disease_May_Have_Cytogenetic_Abnormality	Loss of Chromosome 3p
Some Disease_May_Have_Cytogenetic_Abnormality	Loss of Chromosome 11p
Some Disease_May_Have_Cytogenetic_Abnormality	Loss of Chromosome 12q
Some Disease_May_Have_Cytogenetic_Abnormality	Loss of Chromosome 1p
Some Disease_May_Have_Cytogenetic_Abnormality	Loss of Chromosome 9p
Some Disease_May_Have_Cytogenetic_Abnormality	Gain of Chromosome 3q
Some Disease_May_Have_Cytogenetic_Abnormality	Gain of Chromosome 6p
Some Disease_May_Have_Cytogenetic_Abnormality	Gain of Chromosome 17q22-q24
Some Disease_May_Have_Cytogenetic_Abnormality	Gain of Chromosome 3q
Some Disease_May_Have_Cytogenetic_Abnormality	Gain of Chromosome 20q13
Some Disease_May_Have_Cytogenetic_Abnormality	Gain of Chromosome 7p

Breast Carcinoma Metastatic to the Skin

All Disease_Has_Metastatic_Anatomic_Site	Skin
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Other Examples Applying the Model

Note: Only selected roles/values are shown, to illustrate various aspects.

Most roles/values here would be inherited from parent categories, not asserted directly at this level.

Metastatic Carcinoma to the Lung

Some	Disease_Has_Associated_Anatomic_Site	Lung
All	Disease_Has_Metastatic_Anatomic_Site	Lung
Some	Disease_Has_Primary_Anatomic_Site	Liver
Some	Disease_Has_Primary_Anatomic_Site	Prostate

Prostate Carcinoma Metastatic to the Lung

Some	Disease_Has_Associated_Anatomic_Site	Prostate
Some	Disease_Has_Associated_Anatomic_Site	Lung
All	Disease_Has_Primary_Anatomic_Site	Prostate
All	Disease_Has_Metastatic_Anatomic_Site	Lung

Gastrointestinal Stromal Tumor

All	Disease_Has_Primary_Anatomic_Site	Gastrointestinal Tract
All	Disease_Has_Normal_Cell_Origin	Interstitial Cell of Cajal
All	Disease_Has_Molecular_Abnormality	C-KIT Gene Rearrangement
All	Disease_Has_Molecular_Abnormality	KIT Receptor Tyrosine Kinase Protein (CD117) Overexpression

[one or both values]

Some	Disease_May_Have_Abnormal_Cell	Neoplastic Epithelioid Cell
Some	Disease_May_Have_Abnormal_Cell	Spindle Cell

[neither, one, or both values]

Some	Disease_May_Have_Cytogenetic_Abnormality	Monosomy of Chromosome 14
Some	Disease_May_Have_Cytogenetic_Abnormality	Loss of Chromosome 22

Extraskelatal Myxoid Chondrosarcoma

All	Disease_Has_Normal_Cell_Origin	Chondrocyte
All	Disease_Has_Abnormal_Cell	Neoplastic Chondrocyte
All	Disease_Has_Normal_Tissue_Origin	Soft Tissue
All	Disease_Has_Finding	Non-Encapsulated Neoplasm
All	Disease_Has_Finding	Multinodular Pattern
All	Disease_Has_Finding	Chondromyxoid Stroma

[important typical value]

Some	Disease_Has_Finding	Pain
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[neither, one, or both values]

Some	Disease_May_Have_Abnormal_Cell	Neoplastic Epithelioid Cell
Some	Disease_May_Have_Abnormal_Cell	Rhabdoid Cell

[neither or one group of values]

Group 1

Some	Disease_May_Have_Cytogenetic_Abnormality	t(9;22)(q22;q12) Chromosomal Translocation
Some	Disease_May_Have_Molecular_Abnormality	Fusion Gene NR4A3/EWS Expression
Some	Disease_May_Have_Molecular_Abnormality	Fusion Protein NR4A3/EWS Expression

Group 2

Some	Disease_May_Have_Cytogenetic_Abnormality	t(9;17)(q22;q11) Chromosomal Translocation
Some	Disease_May_Have_Molecular_Abnormality	Fusion Gene NR4A3/RBP56 Expression
Some	Disease_May_Have_Molecular_Abnormality	Fusion Protein NR4A3/ RBP56 Expression

Group 3

Some	Disease_May_Have_Cytogenetic_Abnormality	t(9;15)(q22;q21)
Some	Disease_May_Have_Molecular_Abnormality	Fusion Gene NR4A3/TCF12 Expression
Some	Disease_May_Have_Molecular_Abnormality	Fusion Protein NR4A3/TCF12 Expression

Lacrimal Gland Pleomorphic Adenoma

Some	Disease_Has_Associated_Anatomic_Site	Lacrimal Gland
All	Disease_Has_Primary_Anatomic_Site	Lacrimal Gland
All	Disease_Has_Normal_Tissue_Origin	Glandular Epithelium
All	Disease_Has_Normal_Tissue_Origin	Connective Tissue
All	Disease_Has_Normal_Cell_Origin	Glandular Cell
All	Disease_Has_Normal_Cell_Origin	Myoepithelial Cell (Basket Cell)
All	Disease_Has_Abnormal_Cell	Neoplastic Glandular Cell
All	Disease_Has_Abnormal_Cell	Neoplastic Stromal Cell
All	Disease_Has_Abnormal_Cell	Metaplastic Myoepithelial Cell
Some	Disease_May_Have_Finding	Squamous Metaplasia
Some	Disease_May_Have_Finding	Myxoid Stroma Formation
Some	Disease_May_Have_Finding	Chondromyxoid Stroma Formation

Add Role?

All	Disease_Has_Modifier	Metaplasia
All	Disease_Has_Modifier	Encapsulated